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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/645,337	08/25/2000	KEQIANG WU	104107.01	5854

25944 7590 05/08/2002

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EXAMINER	
MEHTA, ASHWIN D	
ART UNIT	**PAPER NUMBER**
1638	13

DATE MAILED: 05/08/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/645,337	Applicant(s) WU ET AL.	
	Examiner Ashwin Mehta	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2000*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21,23,25,27 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21,23,25,27 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-9 and 11-20, and SEQ ID NO: 3 in Paper No. 9 acknowledged. The traversal is on the ground(s) that SEQ ID NOs: 1-4 represent members of the histone deacetylase family, that SEQ ID NOs: 1 and 2 share high sequence homology, that SEQ ID NOs: 3 and 4 share high sequence homology, and that therefore the non-elected sequences would be encountered when searching the SEQ ID NO: 3 (response, page 2, first, second, and third full paragraphs; it is assumed that Applicants are referring to SEQ ID NOs: 2, 4, 6, and 8, which are encoded by SEQ ID NOs: 1, 3, 5, and 7, respectively). It is noted that histone deacetylases of SEQ ID NOs: 2 and 4 belong to a different family than those of SEQ ID NOs: 6 and 8 (specification, page 14, lines 12-31). However, it is noted that the nucleotide sequences of SEQ ID NOs: 1, 3, 5, and 7 were searched and examined in parent application 09/383,971 (abandoned). Therefore, upon further consideration SEQ ID NOs: 1, 3, 5, and 7 shall be examined here. Applicants also argue that the subject matter of all Groups I-VI are sufficiently related that a search for the subject matter for any one group will encompass all of them, and that search and examination of all the groups would not impose a serious burden (response, page 2, fourth full paragraph and the paragraph bridging pages 2-3). This is not found persuasive because a search for the amino acid sequences, of Group II for example, would not necessarily provide information on the genes encoding them. Further, the method of Group I involves repressing the expression of a targeted gene. The methods of the other groups have different purposes. The methods of the non-elected groups would result in the repression of

unknown, non-targeted genes, resulting in unpredictable phenotypes and results, or the methods are to be used to identify DNA binding proteins. The methods of the non-elected groups involve steps not required for the method of Group I, and produce different results.

Group I, claims 1-9 and 11-20, and SEQ ID NOs: 1, 3, 5, and 7 are examined in this Office action. Claims 10, 21, 23, and 25, 27, and 28 are withdrawn for being drawn to non-elected inventions and require cancellation. The requirement is still deemed proper and is therefore made FINAL.

Drawings

2. Figure 19C, submitted 15 November 2000, is approved for examination. However, see the accompanying PTO-948 for the draftsperson's review.

Also, note that that the following information for effecting drawing changes replaces the information that appears on back of the PTO-948.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

3. **Correction of Informalities -- 37 CFR 1.85**

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

4. **Corrections other than Informalities Noted by Draftsperson on form PTO-948.**

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

5. **Timing of Corrections**

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in **ABANDONMENT** of the application.

Specification

6. The specification fails to comply with the sequence rules of 37 CFR 1.821-1.825. The sequences that appear in Figures 3 and 4 should be referred to, in the brief descriptions of those figures on page 7, by their SEQ ID NOs.

Claim Objections

7. Claims 1, 14 and 15 are objected to because of the following informalities: In claim 1, line 7, "deaceytlase" is misspelled. Claims 14 and 15 are missing the period punctuation mark. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-9 and 11-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation "a nucleotide sequence encoding histone deacetylase and a DNA binding protein" in lines 6-7 of claim 1 renders the claims indefinite. The recitation does not clearly indicate whether or not the histone deacetylase and the DNA binding protein form a fusion protein. It is suggested that the claims be amended to indicate that they do, as this is what the specification teaches (for example at page 26, lines 19-24).

Claim 9 is indefinite for being a "Markush"-type claim and employing incorrect Markush terminology. The following amendments are suggested: in lines 2, 4, and 6, insert --or-- before "SEQ ID NO: 7"; in line 3, insert --or-- before "fragment"; and replace the comma in line 7 with a semi-colon.

Further regarding claims 4 and 9: the term "derivative" in line 3 of the claims also render them indefinite. It is not exactly clear what is meant by this term. The metes and bounds of the claims are not clear.

Claim 20 is indefinite for being dependent on a non-elected claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-9 and 11-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn towards an isolated nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, and SEQ ID NO: 7; any analog, derivative, fragment of said SEQ ID NOs; and any nucleotide sequence that hybridizes to said SEQ ID NOs, wherein said analog, derivative, fragment, and hybridizing sequence encodes a product that exhibits repression of gene expression activity; a chimeric construct comprising said nucleotide sequence; a transgenic plant or seed comprising said nucleotide sequence; a method of regulating gene expression in a transgenic plant comprising introducing into a plant a first chimeric nucleotide sequence comprising a first regulatory element operably associated with a gene of interest, and a controlling sequence, and a second chimeric nucleotide sequence comprising a second regulatory sequence operably associated with a nucleotide sequence encoding a histone deacetylase and a DNA binding domain; or said method wherein said histone deacetylase is selected from the group consisting of AtRPD3A, AtRPD3B, AtHD2A, and AtHD2B, any analog, derivative, or fragment thereof, or any sequence that hybridizes to AtRPD3A, AtRPD3B, AtHD2A, and AtHD2B.

The specification indicates that cDNA clones (SEQ ID NOs: 1, 3, 5, and 7) encoding the *Arabidopsis thaliana* histone deacetylases AtRPD3A, AtRPD3B, AtHD2A, and AtHD2B, (SEQ ID NOs: 2, 4, 6, and 8, respectively), were isolated (page 36, line 22 to page 38, line 8). The specification describes the construction of effector plasmids that comprised a promoter operably

linked to the nucleotide sequence (SEQ ID NO: 1) encoding AtRPD3A or (SEQ ID NO: 5) AtHD2A, fused to the coding region of the DNA-binding domain of GAL4. The effector plasmid, along with a reporter plasmid comprising the GUS coding region operably linked to a promoter and two upstream activating sequences that are bound by the GAL4 protein, were introduced into tobacco leaves by particle bombardment (page 39, lines 20 to page 41, line 2). Reduced GUS activity was observed in leaves comprising the effector and reporter plasmids compared to control leaves that were bombarded with the reporter plasmid and a plasmid that did not comprise AtRPD3A or AtHD2A coding sequences (page 41, lines 6-22). Repression of GUS activity was also observed with effector plasmids that comprised nucleotide sequences that encoded amino acids 1-211 or 1-162 of AtHD2A. Deletion of amino acids 73-245 or 101-245 abolished the repression activity of AtHD2A in this assay (page 41, line 24 to page 42, line 2).

However, the specification does not describe the nucleotide sequence of any analog, derivative, or other fragments of SEQ ID NOs: 1, 3, 5, and 7. The specification indicates that an analog can be any substitution, deletion or addition to the sequence of the histone deacetylase of the present invention, and has the activity of repressing gene expression (page 17, lines 28-31). However, the specification does not describe how the structures of SEQ ID NOs: 2, 4, 6, and 8 can be changed without affecting their functional activity, with the exception of the two fragments of SEQ ID NO: 6 (AtHD2A) discussed above. The specification indicates that the RPD-3 family of histone deacetylases shares a highly-homologous N-terminal domain required for its deacetylase activity, and a more variable short C-terminal region (page 14, lines 12-22). Other functional domains besides the highly homologous "deacetylase domain" are not described, and the function of the C-terminal regions of the proteins is also not described. The

specification also indicates that the other histone deacetylase families, including HD2, do not share homology with the RPD3 family (page 14, lines 22-26). The specification does not describe any other structures besides those of SEQ ID NOs: 1, 3, 5, and 7 that are correlated with the activity of repressing transcription. Further, the analogs apparently do not have to repress gene expression by repressing transcription. The specification, however, does not correlate any other gene expression repression activity with SEQ ID NOs: 2, 4, 6, and 8. The specification also indicates that analogs include DNA sequences that hybridize under stringent hybridization conditions to any one of SEQ ID NOs: 1, 3, 5, or 7 and maintain at least one property of the histone deacetylase (page 18, lines 4-9). However, the specification does not define the stringency of the hybridization conditions, and any two nucleotide sequences can bind to one another, given the appropriate stringency conditions.

Further, the specification does not describe any nucleotide sequences which hybridize under the conditions listed in claims 4 and 9 which repress gene expression in a manner other than that of the amino acid sequences encoded by SEQ ID NOs: 1, 3, 5, and 7. The hybridization conditions described in the claims do not include the stringency of the wash conditions. Therefore, any nucleotide sequence is encompassed by the claims. It is suggested that the wash conditions stated in the specification at page 18, lines 20-21 be inserted into claims 4 and 9. Also see Fiers vs. Sugarno, 25 USPQ 2d (CAFC 1993) at 1606, which states that "[a]n adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself". Given the breadth of the claims encompassing nucleotide sequences that encode any analog, derivative, or fragment of SEQ ID NOs: 1, 3, 5, and 7, and nucleotide sequences that

hybridize to SEQ ID NOs: 1, 3, 5, and 7, that repress gene expression by any mechanism, and lack of guidance as discussed above, the specification fails to provide an adequate written description of the multitude of nucleotide sequences encompassed by the claims.

10. Claims 1-9 and 11-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NOs: 1, 3, 5 and 7, and a method of regulating gene expression in a transgenic plant wherein transcription is repressed, said method comprising SEQ ID NOs: 1, 3, 5, and 7, and or a nucleotide sequence encoding amino acids 1-211 or 1-162 of SEQ ID NO: 6, does not reasonably provide enablement for any other method of regulating gene expression in a transgenic plant with nucleotide sequences encoding histone deacetylases or analogs, derivatives, other fragments of SEQ ID NOs: 1, 3, 5, and 7, or nucleotide sequences that hybridize to SEQ ID NOs: 1, 3, 5, and 7. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are broadly drawn towards an isolated nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, and SEQ ID NO: 7; any analog, derivative, fragment of said SEQ ID NOs; and any nucleotide sequence that hybridizes to said SEQ ID NOs, wherein said analog, derivative, fragment, and hybridizing sequence encodes a product that exhibits repression of gene expression activity; a chimeric construct comprising said nucleotide sequence; a transgenic plant or seed comprising said nucleotide sequence; a method of regulating gene expression in a transgenic plant comprising introducing into a plant a first chimeric nucleotide sequence comprising a first regulatory element operably associated with

a gene of interest, and a controlling sequence, and a second chimeric nucleotide sequence comprising a second regulatory sequence operably associated with a nucleotide sequence encoding a histone deacetylase and a DNA binding domain; or said method wherein said histone deacetylase is selected from the group consisting of AtRPD3A, AtRPD3B, AtHD2A, and AtHD2B, any analog, derivative, or fragment thereof, or any sequence that hybridizes to AtRPD3A, AtRPD3B, AtHD2A, and AtHD2B.

As discussed above, the specification teaches the isolation of four *Arabidopsis* cDNA clones, SEQ ID NOs: 1,3, 5, and 7, which encode the histone deacetylases AtRPD3A (SEQ ID NO: 2), AtRPD3B (SEQ ID NO: 4), AtHD2A (SEQ ID NO: 6), and AtHD2B (SEQ ID NO: 8), respectively. Histone deacetylases repress transcriptional activity. The specification teaches that the nucleotide sequence encoding AtRPD3A or AtHD2A was fused to the coding sequence for the GAL4 DNA-binding domain and placed into an effector plasmid, which was then inserted into tobacco leaves along with a reporter plasmid comprising the GUS coding region operatively linked to a promoter which comprised the GAL4 upstream activating sequence, which is bound by GAL4. GUS expression from the reporter plasmid was repressed when inserted into the plant leaves along with an effector plasmid. Deletions of AtHD2A that left only amino acids 1-211 or 1-162 intact did not affect the repression of GUS activity of intact AtHD2A. The specification also teaches that when a transgenic plant comprising the reporter construct is crossed with a transgenic plant comprising an effector construct in which the AtHD2A-GAL4 fusion is operably linked to the seed-specific NAP promoter, progeny plant are produced that express GUS in leaves, but not in seed, since the AtHD2A-GAL4 fusion protein is expressed in seeds but not in

leaves (page 31, lines 4-18). The same results were obtained when the two constructs were sequentially transformed into the same plant (page 31, line 20 to page 32, line 2).

However, the only manner in which histone deacetylases may regulate gene expression that is enabled by the specification is by repressing gene transcription. The specification at page 1, lines 16-17, admits that histone deacetylation is thought to result in repression of transcription. Neither the specification nor the prior art teaches the involvement of histone deacetylation in any other manner of regulating gene expression. In the absence of further guidance, undue experimentation would be required by one skilled in the art to determine how the claimed nucleotide sequences would regulate gene expression other than by repressing transcription. See also Genentech, Inc. V. Novo Nordisk, A/S, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention. It is suggested that the recitation "regulating gene expression" in line 1 of claim 1 be replaced with --repressing transcription of a gene of interest--.

The specification also does not teach analogs, derivatives, and fragments of SEQ ID NOs: 1, 3, 5, and 7, other than the sequence encoding amino acids 1-211 and 1-162, that retain the histone deacetylase and transcriptional repression activity of SEQ ID NOs: 2, 4, 6, and 8. The specification teaches that analogs can be any substitution, deletion or addition to the sequence of the histone deacetylase of the present invention, and has the activity of repressing gene expression (page 17, lines 28-31). However, the specification does not teach what amino acid sequences can be changed without affecting the functional activity of SEQ ID NO: 2, 4, 6, or 8. In the absence of further guidance, undue experimentation would be required by one skilled in the art to determine how the sequences of SEQ ID NOs: 2, 4, 6, and 8 can be changed

without affecting its enzymatic activity. Khochbin et al. (FEBS Lett., 1997, Vol. 419, pages 157-160) teach that the divergent C-terminus of histone deacetylases may be involved in the targeting of the deacetylase to a particular corepressor complex (page 160). The specification does not teach how the C-termini of SEQ ID NOs: 2, 4, 6, and 8 may be changed without affecting their functional activity and functional specificity. The specification also indicates that analogs include DNA sequences that hybridize under stringent hybridization conditions to any one of SEQ ID NOs: 1, 3, 5, or 7 and maintain at least one property of the histone deacetylase (page 18, lines 4-9). However, this definition encompasses any stringency condition, and therefore encompasses nucleotide sequences that are not related to SEQ ID NOs: 1, 3, 5, or 7, and which do not have all of the properties of SEQ ID NOs: 1, 3, 5, and 7.

The specification also does not teach nucleotide sequences that hybridize with SEQ ID NOs: 1, 3, 5, or 7 under the conditions stated in claims 4 and 9, that also retain their respective activities. The conditions in the claims do not include the wash conditions that define the level of stringency of the hybridization. The claims then encompass nucleotide sequences that are unrelated to SEQ ID NOs: 1, 3, 5, and 7. Further, as discussed above, members of the different histone deacetylase families share high homology in their N-termini. Therefore, the hybridizing sequences may hybridize due to homologies at the 5' end of their nucleotide sequences, but may still have different functional specificities. Further, the sequences as claimed can have any type of activity of repressing gene expression. However, the specification does not teach one how to use such nucleotide sequences with the disclosed invention. See Genentech, Inc. V. Novo Nordisk, A/S, *supra*. Given the breadth of the claims encompassing a method for any type of regulation of gene expression in plants, and analogs, derivatives, fragments, and nucleotide

sequences that hybridize to SEQ ID NO: 1, 3, 5, and 7 that may repress gene expression by any mechanism, the unpredictability of the art and lack of guidance as discussed above, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

11. Claim 9 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by Tomihama et al.

The claim is broadly drawn towards any isolated nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7; any analog,

derivative, fragment of said SEQ ID NOs; and any nucleotide sequence that hybridizes to said SEQ ID NOs, wherein said analog, derivative, fragment, and hybridizing sequence encodes a product that exhibits repression of gene expression activity.

Tomihama et al. teach the nucleotide sequence of SEQ ID NO: 1. The sequence was deposited with Genbank under Accession No. AF014824 on August 12, 1997. The property of repression of gene expression activity is inherent to the sequence.

12. Claims 9, 11, and 17-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Baldwin et al. (U.S. Patent No. 6,287,843).

The claims are broadly drawn towards any isolated nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7; any analog, derivative, or fragment of said SEQ ID NOs, and any nucleotide sequence that hybridizes to said SEQ ID NOs, wherein said analog, derivative, fragment, and hybridizing sequence encodes a product that exhibits repression of gene expression activity; or a chimeric construct comprising a regulatory element operatively associated with said isolated nucleotide sequence; or a vector comprising said chimeric construct; a transgenic plant, plant cell, or seed comprising said isolated nucleotide sequence.

Baldwin et al. teach isolated maize cDNA clones encoding histone deacetylases (col. 18, line 63 to col. 21, line 42; claims). The nucleotide sequences and their encoded proteins taught by Baldwin et al. are analogs of instant SEQ ID NOs: 1, 3, 5, and 7, as additions, substitutions, and deletions of sequences of SEQ ID NOs: 1, 3, 5, or 7 are considered analogs (instant specification, page 17, lines 28-31). Additions, substitutions, or deletions of instant SEQ ID

NOs: 1, 3, 5, or 7 yield the cDNAs encoding the histone deacetylases taught by Baldwin et al. Baldwin et al. also teach plant expression vectors comprising the cloned histone deacetylase sequence placed under the transcriptional control of promoters, such as the maize ubiquitin promoter (col. 21, lines 46-49; claims), which is constitutive. The expression vector was transformed into immature maize embryos by particle bombardment. Baldwin et al. also teach transgenic plants regenerated from the transformed embryos, seed of transgenic plants (col. 21, line 50 to col. 22, line 44; claims).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 1-9 and 11-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al. (WO 98/48825) in combination with Baldwin et al.

The claims are broadly drawn towards an isolated nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, and SEQ ID NO: 7; any analog, derivative, fragment of said SEQ ID NOs; and any nucleotide sequence that hybridizes to said SEQ ID NOs, wherein said analog, derivative, fragment, and hybridizing sequence encodes a product that exhibits repression of gene expression activity; a chimeric construct comprising said nucleotide sequence; a transgenic plant or seed comprising said nucleotide sequence; a

method of regulating gene expression in a transgenic plant comprising introducing into a plant a first chimeric nucleotide sequence comprising a first regulatory element operably associated with a gene of interest, and a controlling sequence, and a second chimeric nucleotide sequence comprising a second regulatory sequence operably associated with a nucleotide sequence encoding a histone deacetylase and a DNA binding domain; or said method wherein said histone deacetylase is selected from the group consisting of AtRPD3A, AtRPD3B, AtHD2A, and AtHD2B, any analog, derivative, or fragment thereof, or any sequence that hybridizes to AtRPD3A, AtRPD3B, AtHD2A, and AtHD2B.

Evans et al. teach fusing the nucleotide sequence encoding the histone deacetylase HDAC1 to the coding sequence for the GAL5 DNA-binding domain (DBD) and transfecting it into CV-1 cells with a reporter gene that comprised GAL4 binding sites upstream of minimal TK promoter fused to luciferase coding sequence. The HDAC1-GAL4 fusion repressed luciferase activity by 60-fold compared to the basal level of activity of the TK promoter (page 27, line 23 to page 28, line 3).

Evans et al. do not teach transformed plant cells.

Baldwin et al. is discussed above.

It would have been obvious and within the scope of one of ordinary skill in the art at the time the invention was made to modify the method of repressing transcription of Evans et al. by introducing the histone deacetylase/GAL4 DBD fusion and reporter gene constructs into plant cells. Any appropriate method of transformation could have been used, including the particle bombardment of maize embryos and regeneration of transgenic plants taught by Baldwin et al. It was also obvious that the HDAC1 coding sequence taught by Evans et al. could have been

replaced with other histone deacetylase coding sequences, such as the maize cDNAs taught by Baldwin et al. It would have been obvious that the histone deacetylase/GAL4 and the reporter gene constructs could have been placed on the same vector, or placed on different vectors and transformed into plants simultaneously or sequentially. It also would have been obvious to transform the two vectors into different plants and subsequently cross the plants. It was obvious that any of these methods of bringing the two vectors into the same plant cell could have been used, and are just an optimization of process parameters. One would have been motivated to introduce the histone deacetylase/GAL4 DNA binding domain fusion construct and the construct comprising the reporter gene and GAL4 binding site/promoter construct into plants, as Evans et al. demonstrate the successful use of this system to down regulate gene transcription, and to use this system of regulation to control transgene expression in crop plants. It also would have been obvious to collect seed from the transgenic plants for the purpose of propagation.

14. No claim is allowed.

Contact Information

Any inquiry concerning this or earlier communications from the examiner should be directed to Ashwin Mehta, whose telephone number is 703-306-4540. The examiner can normally be reached on Mondays-Thursdays and alternate Fridays from 8:00 A.M to 5:30 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at 703-306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 and 703-872-9306 for regular

communications and 703-872-9307 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

A.M.
May 2, 2002

DAVID T. FOX
PRIMARY EXAMINER
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